

10/666722

***** INVENTOR RESULTS *****

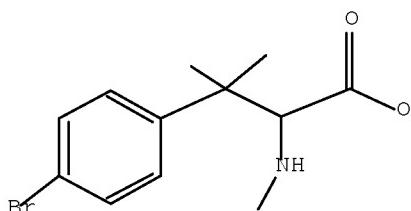
(ALSO SEARCH RESULTS FOR COMPOUND IN EXAMPLE 57/CLAIM 73 AND CANCER TUMORS)
=> d his 143

(FILE 'HCAPLUS' ENTERED AT 14:11:40 ON 05 MAR 2009)

L43 3 S L41 OR L22
 SAVE L43 JEA722HCAIN/A
 DEL JEA722HCAIN/A
 SAVE TEMP L43 JEA722HCAIN/A
 SAVE TEMP L35 JEA722HCAP/A

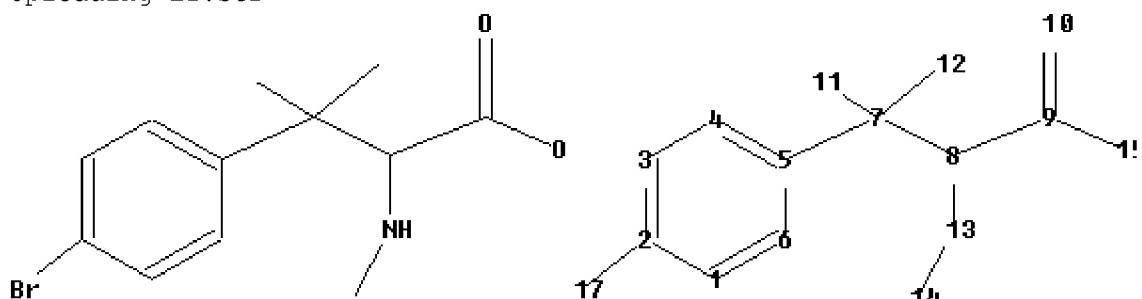
FILE 'STNGUIDE' ENTERED AT 14:20:39 ON 05 MAR 2009

=> d que 143
L6 STR



Structure attributes must be viewed using STN Express query preparation:

Uploading L1.str



chain nodes :
7 8 9 10 11 12 13 14 15 17
ring nodes :
1 2 3 4 5 6
chain bonds :
2-17 5-7 7-8 7-11 7-12 8-9 8-13 9-10 9-15 13-14
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
8-13 9-10 9-15 13-14
exact bonds :
2-17 5-7 7-8 7-11 7-12 8-9
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

Match level :

 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 17:CLASS

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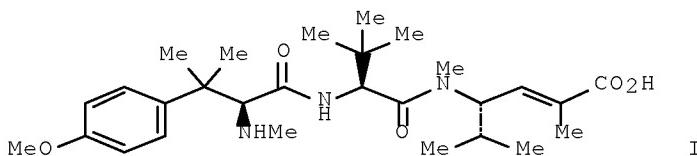
L8      88 SEA FILE=REGISTRY ABB=ON PLU=ON TETRAMETHYL (L) VALINAMID?
L9      26 SEA FILE=REGISTRY ABB=ON PLU=ON L8 (L) TYROSYL
L11     21 SEA FILE=REGISTRY ABB=ON PLU=ON L9 (L) BUTENYL
L12     16 SEA FILE=REGISTRY ABB=ON PLU=ON L11 (L) DIMETHYL?
L13      8 SEA FILE=REGISTRY ABB=ON PLU=ON L12 (L) CARBOXY
L14      3 SEA FILE=REGISTRY SSS FUL L6
L15      2 SEA FILE=HCAPLUS ABB=ON PLU=ON L13
L16      3 SEA FILE=HCAPLUS ABB=ON PLU=ON L14
L17      3 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 OR L16
L21    167483 SEA FILE=HCAPLUS ABB=ON PLU=ON NEOPLASM/CT
L22      3 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND L21
L23      1 SEA FILE=HCAPLUS ABB=ON PLU=ON US20040121965/PN
L36      84 SEA FILE=HCAPLUS ABB=ON PLU=ON GREENBERGER L?/AU
L37      34 SEA FILE=HCAPLUS ABB=ON PLU=ON LOGANZO F?/AU
L38      8 SEA FILE=HCAPLUS ABB=ON PLU=ON DISCAFANI MARRO C?/AU OR
          MARRO C?/AU
L39      83 SEA FILE=HCAPLUS ABB=ON PLU=ON ZASK A?/AU
L40      61 SEA FILE=HCAPLUS ABB=ON PLU=ON AYRAL KALOUSTIAN S?/AU OR
          KALOUSTIAN S?/AU
L41      3 SEA FILE=HCAPLUS ABB=ON PLU=ON (((L36 OR L37 OR L38 OR L39
          OR L40)) AND L16) OR (L16 AND L23)
L43      3 SEA FILE=HCAPLUS ABB=ON PLU=ON L41 OR L22

```

=> d 143 1-3 ibib abs hitstr hitind

L43 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:617803 HCAPLUS Full-text
 DOCUMENT NUMBER: 141:314607
 TITLE: Synthesis and Biological Activity of Analogues of the
 Antimicrotubule Agent
 N, β , β -Trimethyl-L-phenylalanyl-N1-[(1S,2E)-3-
 carboxy-1-isopropylbut-2-enyl]-
 N1,3-dimethyl-L-valinamide (HTI-286)
 Zask, Arie; Birnberg, Gary; Cheung,
 Katherine; Kaplan, Joshua; Niu, Chuan; Norton, Emily;
 Suayan, Ronald; Yamashita, Ayako; Cole, Derek; Tang,
 Zhilian; Krishnamurthy, Girija; Williamson, Robert;
 Khafizova, Gulnaz; Musto, Sylvia; Hernandez, Richard;
 Annable, Tami; Yang, Xiaoran; Discafani, Carolyn;
 Beyer, Carl; Greenberger, Lee M.;
 Loganzo, Frank; Ayrat-Kaloustian,
 Semiramis
 CORPORATE SOURCE: Chemical and Screening Sciences, and Oncology
 Research, Wyeth Research, Pearl River, NY, 10965, USA
 SOURCE: Journal of Medicinal Chemistry (2004), 47(19),
 4774-4786
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 141:314607

GI



AB Hemiasterlin, a tripeptide isolated from marine sponges, induces microtubule depolymerization and mitotic arrest in cells. HTI-286, an analog from an initial study of the hemiasterlins, is presently in clin. trials. In addition to its potent antitumor effects, HTI-286 has the advantage of circumventing the P-glycoprotein-mediated resistance that hampers the efficacy of other antimicrotubule agents such as paclitaxel and vincristine in animal models. This paper describes an in-depth study of the structure-activity relationships (SAR) of analogs of HTI-286, their effects on microtubule polymerization, and their in vitro and in vivo anticancer activity. Regions of the mol. necessary for potent activity are identified. Groups tolerant of modification, leading to novel analogs, are reported. Potent analogs identified through in vivo studies in tumor xenograft models include one superior analog, HTI-042 (I).

IT 676633-19-5
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation of analogs of peptide HTI-286 and SAR study of their anticancer

activity and effects on microtubule polymerization)

RN 676633-19-5 HCPLUS

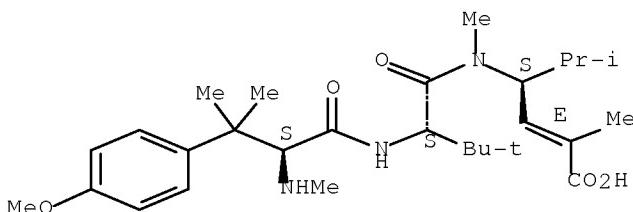
CN L-Valinamide, N,O, β -tetramethyl-L-tyrosyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl-, mono(trifluoroacetate) (9CI)
 (CA INDEX NAME)

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CRN 676633-18-4

CMF C28 H45 N3 O5

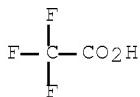
Absolute stereochemistry.
 Double bond geometry as shown.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



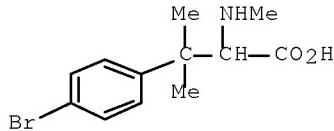
IT 676627-55-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of analogs of peptide HTI-286 and SAR study of their anticancer

activity and effects on microtubule polymerization)

RN 676627-55-7 HCPLUS

CN Phenylalanine, 4-bromo-N, β,β -trimethyl- (CA INDEX NAME)

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

IT Antitumor agents

Human

Neoplasm

(preparation of analogs of peptide HTI-286 and SAR study of their anticancer

activity and effects on microtubule polymerization)

IT 228266-43-1P 228266-45-3P 228266-48-6P 676633-19-5P

676633-61-7P 676633-65-1P 676633-77-5P 676633-80-0P 676633-90-2P

676634-21-2P 676634-47-2P 676634-59-6P 676634-66-5P 676634-77-8P

676634-83-6P 676634-90-5P 676634-93-8P 676635-36-2P 676635-39-5P

676635-58-8P 676636-07-0P 676636-11-6P 676636-15-0P 676636-19-4P

676636-28-5P 676636-79-6P 765930-77-6P 765930-82-3P 765930-86-7P

765930-88-9P 765931-06-4P 765931-11-1P 765931-16-6P 765931-18-8P

765931-22-4P 765931-24-6P 765931-27-9P 765931-29-1P 765931-33-7P

765931-35-9P 765931-39-3P 765931-44-0P 765931-47-3P 765931-49-5P

765931-52-0P 765931-54-2P 765931-56-4P 765931-58-6P 765931-60-0P

765931-62-2P 765931-64-4P 765931-67-7P 765931-71-3P 765931-73-5P

765931-89-3P 765931-91-7P 765931-94-0P 765931-97-3P 765932-00-1P

765932-03-4P 765932-05-6P 765932-08-9P 765932-10-3P 765932-35-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL

(Biological study); PREP (Preparation)

(preparation of analogs of peptide HTI-286 and SAR study of their anticancer

activity and effects on microtubule polymerization)

IT 77586-77-7P 77586-78-8P 228266-34-0P 676627-53-5P

676627-55-7P 676627-63-7P 676628-38-9P 676630-42-5P

676630-45-8P 676636-59-2P 765930-74-3P 765930-79-8P 765930-91-4P

10/666722

765930-93-6P 765930-95-8P 765930-98-1P 765931-01-9P 765932-15-8P
765932-18-1P 765932-20-5P 765932-22-7P 765932-24-9P 765932-26-1P
765932-30-7P 765932-37-4P 845252-69-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of analogs of peptide HTI-286 and SAR study of their anticancer

activity and effects on microtubule polymerization)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 2 OF 3 HCPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:580770 HCPLUS Full-text

DOCUMENT NUMBER: 141:253645

TITLE: Probing the Interaction of HTI-286 with Tubulin Using a Stilbene Analogue

AUTHOR(S): Lo, Mei-Chu; Aulabaugh, Ann; Krishnamurthy, Girija; Kaplan, Joshua; Zask, Arié; Smith, Robert P.; Ellestad, George

CORPORATE SOURCE: Biophysics/Enzymology-Chemical and Screening Sciences, Medicinal Chemistry-Chemical and Screening Sciences, and Vaccines Research, Wyeth Research, Pearl River, NY, 10965, USA

SOURCE: Journal of the American Chemical Society (2004), 126(32), 9898-9899

CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:253645

AB HTI-286 is a synthetic analog of the natural product hemiasterlin. HTI-286 is a potent antitumor agent that induces tubulin oligomerization. To investigate the binding stoichiometry and the binding site during this ligand-induced tubulin association, synthesized an analog of HTI-286 containing the chromophore stilbene was synthesized. Using the distinct UV absorbance of the stilbene analog, the amts. of inhibitors bound to different tubulin oligomers was determined by anal. ultracentrifugation. Herein described are findings based on these expts. At the ratio of inhibitor to protein equal to or greater than 1, the stilbene analog induces oligomerization of tubulin to a ring structure. The binding stoichiometry in the ring is one inhibitor per tubulin monomer (defined as an α/β -heterodimer). At the ratio of inhibitor to protein less than 1, tubulin forms multiple intermediates, with the binding stoichiometry less than one inhibitor per tubulin monomer for all intermediates. The stable complex between the inhibitor and tubulin monomer was not detected under these exptl. conditions. The binding site of the stilbene analog does not overlap with the classic tubulin-binding agent, colchicine.

IT 756894-40-3P

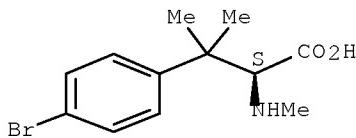
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(interaction of HTI-286 stilbene analog with tubulin)

RN 756894-40-3 HCPLUS

CN L-Phenylalanine, 4-bromo-N, β,β -trimethyl- (CA INDEX NAME)

Absolute stereochemistry.



CC 1-3 (Pharmacology)
 Section cross-reference(s): 34

IT Antitumor agents

 Neoplasm

 Stoichiometry

 Structure-activity relationship

 (interaction of HTI-286 stilbene analog with tubulin)

IT 91133-59-4P 676627-53-5P 676627-58-0P 676635-84-0P
 756894-40-3P 756894-42-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

 (interaction of HTI-286 stilbene analog with tubulin)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:267231 HCAPLUS Full-text

DOCUMENT NUMBER: 140:304081

TITLE: Preparation of peptides for treating resistant tumors

INVENTOR(S): Greenberger, Lee Martin; Loganzo,
 Frank, Jr.; Discafani-Marro, Carolyn Mary
 ; Zasek, Arie; Ayral-Kaloustian,
 Semiramis

PATENT ASSIGNEE(S): Wyeth Holdings Corporation, USA

SOURCE: PCT Int. Appl., 442 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026293	A2	20040401	WO 2003-US29832	20030918
WO 2004026293	A3	20041216		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2406504	A1	20040320	CA 2002-2406504	20021003
AU 2003275126	A1	20040408	AU 2003-275126	20030918
US 20040121965	A1	20040624	US 2003-666722	20030918 <--
PRIORITY APPLN. INFO.:			US 2002-411883P	P 20020920
			WO 2003-US29832	W 20030918

OTHER SOURCE(S): MARPAT 140:304081

AB The invention provides peptides R1R2NCH(CR3R4R5)CONR6CHR7CONR8R9 [R1-R8 are H or an (un)saturated moiety having a linear, branched, or cyclic skeleton containing 1-10 (un)substituted carbon atoms and 0-4 each nitrogen, oxygen, or sulfur atoms; or R1R2N or R3R4C is a 3- to 7-membered ring; R9 is -Y-CO-Z, where Y is alkyl and Z is OH, SH, NH₂, an amino acid residue, etc. (with provisos)] for treating or inhibiting the growth or eradication of tumors which are resistant to at least one chemotherapeutic agent. Thus, N, β , β -trimethyl-L-phenylalanyl-N1-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N1,3-dimethyl-L-valinamide was prepared and shown to be a potent inhibitor of cell growth in 34 tumor cell lines (mean IC₅₀ = 2.1 ± 1.7 nM, median 1.7 nM, range 0.2-7.3 nM) and is distinct from paclitaxel which has an usually large range of activity. The activity is independent of tumor origin and in many cases this peptide is considerably more potent than paclitaxel.

IT 676633-18-4P 676633-19-5P 676633-25-3P

676633-26-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

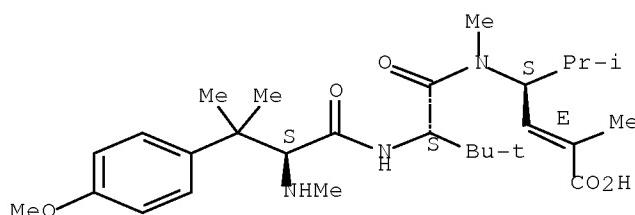
(preparation of peptides for treating resistant tumors)

RN 676633-18-4 HCPLUS

CN L-Valinamide, N,O, β , β -tetramethyl-L-tyrosyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-but enyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



RN 676633-19-5 HCPLUS

CN L-Valinamide, N,O, β , β -tetramethyl-L-tyrosyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-but enyl]-N,3-dimethyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

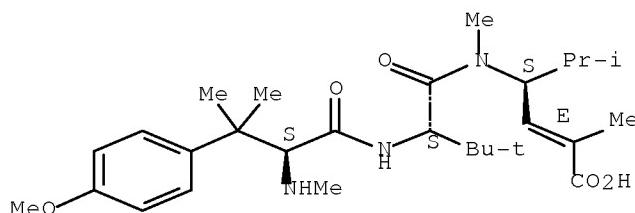
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CRN 676633-18-4

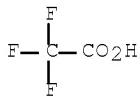
CMF C28 H45 N3 O5

Absolute stereochemistry.

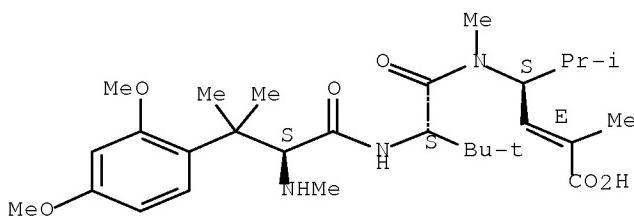
Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2RN 676633-25-3 HCPLUS
CN L-Valinamide, 2-methoxy-N,O, β , β -tetramethyl-L-tyrosyl-N-[$(1S,2E)$ -3-carboxy-1-(1-methylethyl)-2-but enyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

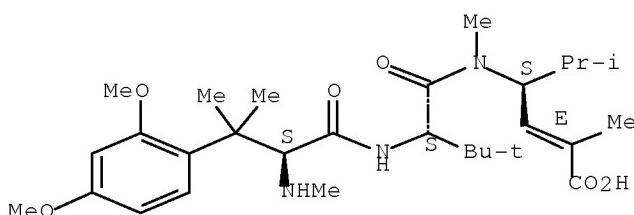
Absolute stereochemistry.
Double bond geometry as shown.

RN 676633-26-4 HCPLUS
CN L-Valinamide, 2-methoxy-N,O, β , β -tetramethyl-L-tyrosyl-N-[$(1S,2E)$ -3-carboxy-1-(1-methylethyl)-2-but enyl]-N,3-dimethyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

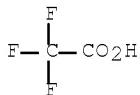
CM 1

CRN 676633-25-3
CMF C29 H47 N3 O6

Absolute stereochemistry.
Double bond geometry as shown.



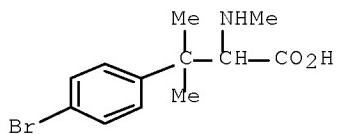
CM 2

CRN 76-05-1
CMF C2 H F3 O2

IT 676627-55-7P 676627-67-1P 676628-10-7P
 676628-16-3P 676629-10-0P 676629-16-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of peptides for treating resistant tumors)

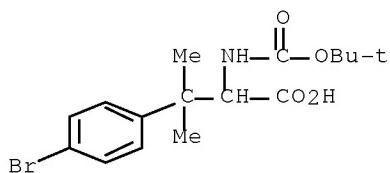
RN 676627-55-7 HCPLUS

CN Phenylalanine, 4-bromo-N, β,β -trimethyl- (CA INDEX NAME)



RN 676627-67-1 HCPLUS

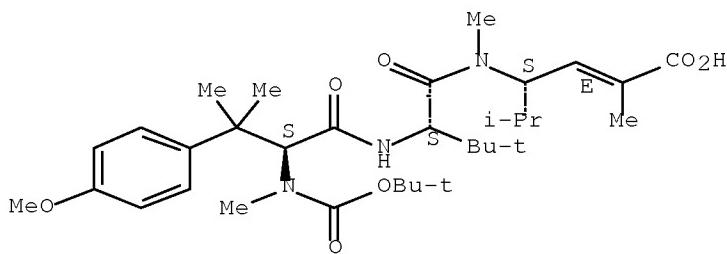
CN Phenylalanine, 4-bromo-N-[(1,1-dimethylethoxy)carbonyl]- β,β -dimethyl- (CA INDEX NAME)



RN 676628-10-7 HCPLUS

CN L-Valinamide, N-[(1,1-dimethylethoxy)carbonyl]-N,O, β,β -tetramethyl-L-tyrosyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

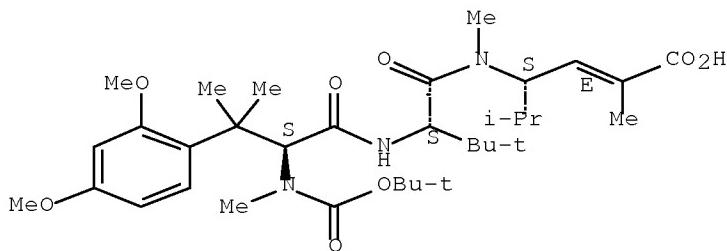


RN 676628-16-3 HCPLUS

CN L-Valinamide, N-[(1,1-dimethylethoxy) carbonyl]-2-methoxy-N,O,β,β-tetramethyl-L-tyrosyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-but enyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

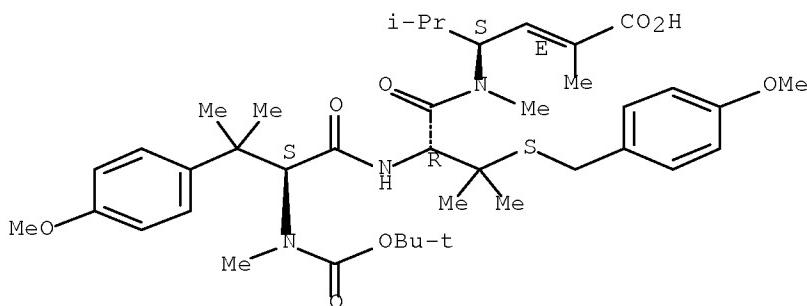


RN 676629-10-0 HCPLUS

CN L-Valinamide, N-[(1,1-dimethylethoxy) carbonyl]-N,O,β,β-tetramethyl-L-tyrosyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-but enyl]-3-[(4-methoxyphenyl)methyl]thio]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

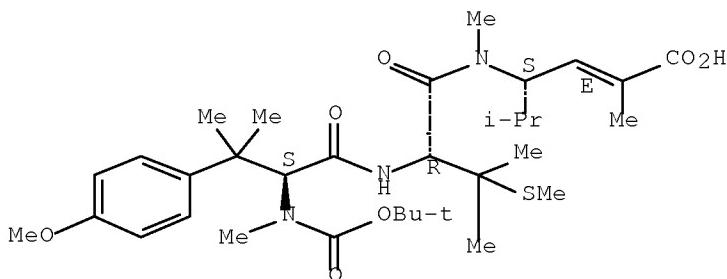
Double bond geometry as shown.



RN 676629-16-6 HCPLUS

CN L-Valinamide, N-[(1,1-dimethylethoxy) carbonyl]-N,O,β,β-tetramethyl-L-tyrosyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-but enyl]-N-

Absolute stereochemistry.
Double bond geometry as shown.



IC ICM A61K031-191
ICS A61K031-194; A61P035-00; A61K031-192; A61K031-195

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

IT Antitumor agents

Neoplasm

(preparation of peptides for treating resistant tumors)

IT	169181-24-2P	228266-42-0P	228266-48-6P	228266-49-7P	500229-47-0P
	676631-37-1P	676631-40-6P	676631-42-8P	676631-44-0P	676631-47-3P
	676631-50-8P	676631-52-0P	676631-55-3P	676631-57-5P	676631-60-0P
	676631-61-1P	676631-65-5P	676631-68-8P	676631-74-6P	676631-76-8P
	676631-81-5P	676631-84-8P	676631-88-2P	676631-89-3P	676631-91-7P
	676631-92-8P	676631-97-3P	676632-00-1P	676632-05-6P	676632-08-9P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptides for treating resistant tumors)

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of peptides for treating resistant tumors)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/666722

***** QUERY RESULTS *****
(COMPOUNDS FROM CLAIM 28-51 AND CANCER/TUMOR)

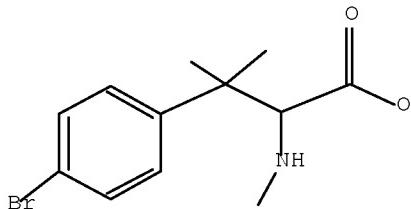
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(FILE 'REGISTRY' ENTERED AT 14:08:02 ON 05 MAR 2009)

FILE 'HCAPLUS' ENTERED AT 14:09:31 ON 05 MAR 2009
L35 4 S L33 NOT L22

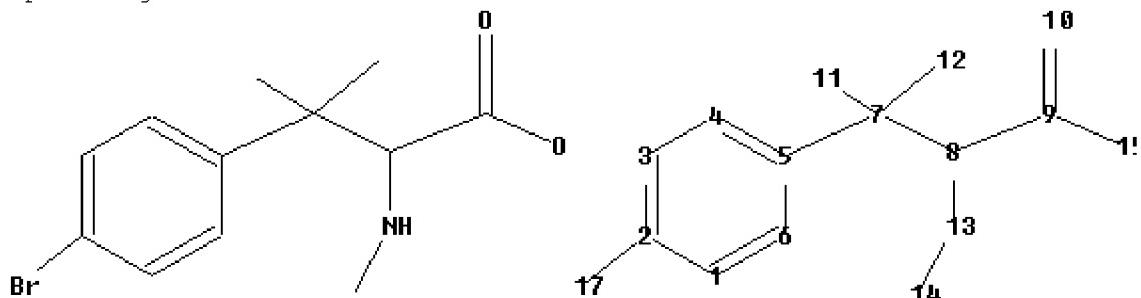
=> d que 135

L6 STR



Structure attributes must be viewed using STN Express query preparation:

Uploading L1.str



chain nodes :

7 8 9 10 11 12 13 14 15 17

ring nodes :

1 2 3 4 5 6

chain bonds :

2-17 5-7 7-8 7-11 7-12 8-9 8-13 9-10 9-15 13-14

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :

8-13 9-10 9-15 13-14

exact bonds :

2-17 5-7 7-8 7-11 7-12 8-9

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

isolated ring systems :

containing 1 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS

11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 17:CLASS

L8 88 SEA FILE=REGISTRY ABB=ON PLU=ON TETRAMETHYL (L) VALINAMID?

L9 26 SEA FILE=REGISTRY ABB=ON PLU=ON L8 (L) TYROSYL

L11 21 SEA FILE=REGISTRY ABB=ON PLU=ON L9 (L) BUTENYL

L12 16 SEA FILE=REGISTRY ABB=ON PLU=ON L11 (L) DIMETHYL?

L13 8 SEA FILE=REGISTRY ABB=ON PLU=ON L12 (L) CARBOXY

L14 3 SEA FILE=REGISTRY SSS FUL L6

L15 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L13

L16 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L14

L17 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 OR L16

L21 167483 SEA FILE=HCAPLUS ABB=ON PLU=ON NEOPLASM/CT

L22 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND L21

L24 566 SEA FILE=REGISTRY ABB=ON PLU=ON (100-66-3/BI OR 100564-78-1/B
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L25 144788 SEA FILE=HCAPLUS ABB=ON PLU=ON L24

L27 151 SEA FILE=HCAPLUS ABB=ON PLU=ON "L() VALINAMIDE"

L28 17 SEA FILE=HCAPLUS ABB=ON PLU=ON L25 AND L27

L29 377 SEA FILE=HCAPLUS ABB=ON PLU=ON VALINAMIDE

L30 35 SEA FILE=HCAPLUS ABB=ON PLU=ON L25 AND L29

L31 35 SEA FILE=HCAPLUS ABB=ON PLU=ON L28 OR L30

L33 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L31 AND (CANCER# OR NEOPLAS?
 OR TUMOR# OR TUMOUR# OR CARCIN?)

L35 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L33 NOT L22

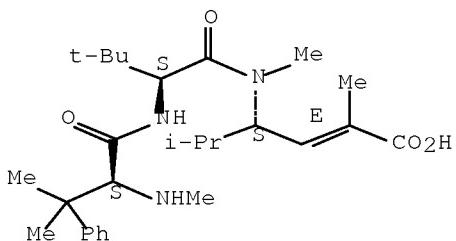
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L35 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2009 ACS on STN

10/666722

ACCESSION NUMBER: 2005:312854 HCPLUS Full-text
DOCUMENT NUMBER: 143:21680
TITLE: Two Photoaffinity Analogues of the Tripeptide,
Hemiassterlin, Exclusively Label α -Tubulin
AUTHOR(S): Nunes, Maria; Kaplan, Joshua; Wooters, Joseph; Hari,
Malathi; Minnick, Albert A., Jr.; May, Michael K.;
Shi, Celine; Musto, Sylvia; Beyer, Carl;
Krishnamurthy, Girija; Qiu, Yongchang; Loganzo, Frank;
Ayal-Kaloustian, Semiramis; Zask, Arie; Greenberger,
Lee M.
CORPORATE SOURCE: Oncology Research, Chemical and Screening Sciences,
Radiosynthesis Group, and Bioorganic Enzymology, Wyeth
Research, Pearl River, NY, 10965, USA
SOURCE: Biochemistry (2005), 44(18), 6844-6857
CODEN: BICAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A synthetic analog of the tripeptide hemiassterlin, designated HTI-286, depolymerizes microtubules, is a poor substrate for P-glycoprotein, and inhibits the growth of paclitaxel-resistant tumors in xenograft models. Two radiolabeled photoaffinity analogs of HTI-286, designated 4-benzoyl-N, β , β -trimethyl-L-phenylalananyl-N1-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N1,3-dimethyl-L-valinamide (probe 1) and N, β , β -trimethyl-L-phenylalananyl-4-benzoyl-N-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N, β , β -trimethyl-L-phenylalaninamide (probe 2), were made to help identify HTI-286 binding sites in tubulin. HTI-286, probe 1, and probe 2 had similar affinities for purified tubulin [apparent KD(app) = 0.2-1.1 μ M], inhibited polymerization of purified tubulin .apprx.80%, and were potent inhibitors of cell growth (IC50 = 1.0-22 nM). Both radiolabeled probes labeled exclusively α -tubulin. Labeling by [3H]probe 1 was inhibited by probe 1, HTI-286, vinblastine, or dolastatin 10 (another peptide antimitotic agent that depolymerizes microtubules) but was either unaffected or enhanced (at certain temps.) by colchicine or paclitaxel. [3H]Probe 1 also labeled exclusively tubulin in cytosolic exts. of whole cells. [3H]Probe 1 also labeled exclusively tubulin in cytosolic exts. of whole cells. The major, if not exclusive, contact site for probe 1 was mapped to residues 314-339 of α -tubulin and corresponds to the sheet 8 and helix 10 region. This region is known to (1) have longitudinal interactions with β -tubulin across the interdimer interface, (2) have lateral interactions with adjacent protofilaments, and (3) contact the N-terminal region of stathmin, a protein that induces depolymn. of tubulin. Binding of probe 1 to this region may alter the conformation of tubulin outside the labeling domain, since enzymic removal of the C-terminus of only α -tubulin by subtilisin after, but not before, photolabeling is blocked by probe 1. These results suggest that hemiassterlin is in close contact with α -tubulin and may span the interdimer interface so that it contacts the vinblastine- and dolastatin 10-binding sites believed to be in β -tubulin. In addition, we speculate that antimitotic peptides mimic the interaction of stathmin with tubulin.
IT 228266-40-8, HTI-286 676634-31-4
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
RN 228266-40-8 HCPLUS
CN L-Valinamide, N, β , β -trimethyl-L-phenylalananyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-but enyl]-N,3-dimethyl-

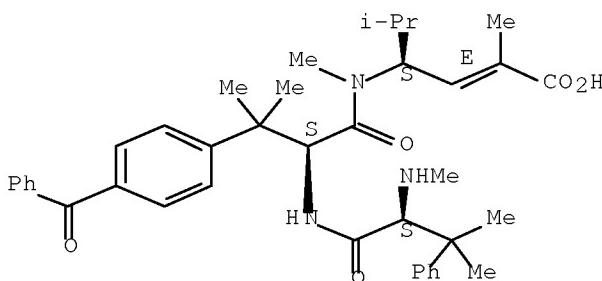
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 676634-31-4 HCPLUS

CN L-Phenylalaninamide, N,β,β-trimethyl-L-phenylalanyl-4-benzoyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-butene]-N,β,β-trimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 6-3 (General Biochemistry)

Section cross-reference(s): 9

IT 228266-40-8, HTI-286 676634-31-4 853013-41-9

RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(two photoaffinity analogs of tripeptide, hemiasterlin, exclusively label α-tubulin)

REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 2 OF 4 HCPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:300201 HCPLUS Full-text

DOCUMENT NUMBER: 142:373856

TITLE: Preparation of quinolines and quinazolines as inhibitors of c-Met and other tyrosine kinases and therapeutic uses against proliferative diseases

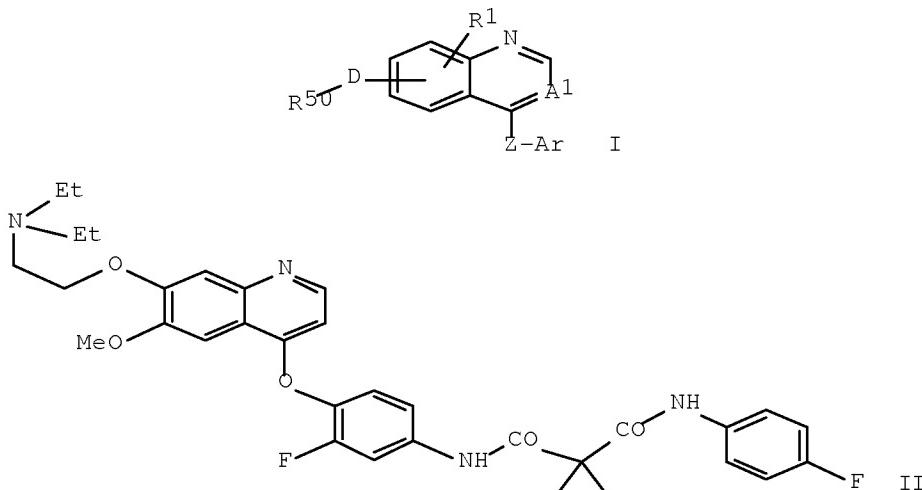
INVENTOR(S): Bannen, Lynne Canne; Chan, Diva Sze-ming; Chen, Jeff; Dalrymple, Lisa Esther; Forsyth, Timothy Patrick; Huynh, Tai Phat; Jammalamadaka, Vasu; Khoury, Richard George; Leahy, James William; Mac, Morrison B.; Mann, Grace; Mann, Larry W.; Nuss, John M.; Parks, Jason

10/666722

PATENT ASSIGNEE(S): Jevious; Takeuchi, Craig Stacy; Wang, Yong; Xu, Wei
 Exelixis, Inc., USA
 SOURCE: PCT Int. Appl., 428 pp.
 CODEN: PIXXD2
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WO 2005030140	A2	20050407	WO 2004-US31523	20040924
WO 2005030140	A3	20050519		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004275842	A1	20050407	AU 2004-275842	20040924
CA 2537812	A1	20050407	CA 2004-2537812	20040924
EP 1673085	A2	20060628	EP 2004-789057	20040924
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2007506777	T	20070322	JP 2006-528265	20040924
US 20070054928	A1	20070308	US 2006-586751	20061026
US 20070225307	A1	20070927	US 2007-753462	20070524
US 20070244116	A1	20071018	US 2007-753503	20070524
PRIORITY APPLN. INFO.:			US 2003-506181P	P 20030926
			US 2004-535377P	P 20040109
			US 2004-577384P	P 20040604
			WO 2004-US31523	W 20040924
			US 2006-573336	B1 20060918
			US 2006-586751	A1 20061026

OTHER SOURCE(S): CASREACT 142:373856; MARPAT 142:373856
 GI



AB The present invention provides compds. (shown as I; variables defined below; e.g. N-[4-[(7-[(2-diethylamino)ethyl]oxy)-6-(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide (shown as II)) for modulating protein kinase enzymic activity for modulating cellular activities such as proliferation, differentiation, programmed cell death, migration and chemoinvasion. More specifically, the invention provides quinazolines and quinolines which inhibit, regulate and/or modulate kinase receptors, particularly c-Met, KDR, c-Kit, flt-3 and flt-4, signal transduction pathways related to the changes in cellular activities as mentioned above, compns. which contain these compds., and methods of using them to treat kinase-dependent diseases and conditions. The present invention also provides methods for making compds. as mentioned above, and compns. which contain these compds. For I: R1 = H, halogen, OR3, NO2, NH2, NR3R4, and (un)substituted lower alkyl; A1 = :N-, :C(H)-, and :C(CN)-; Z = -S(O)0-2-, -O-, and -NR5-; Ar is aryl or heteroaryl; D = -O-, -S(O)0-2-, and -NR15-; R50 = R3 or bicyclic radical; addnl. details are given in the claims. Methods of preparation are claimed and .apprx.80 example preps. of I and intermediates are included. For example, II was prepared (34 %) from 2-(diethylamino)ethanol and cyclopropane-1,1-dicarboxylic acid N-[3-fluoro-4-[(7-hydroxy-6-methoxyquinolin-4-yl)oxy]phenyl]amide N-(4-fluorophenyl)amide, which was prepared (89 %) by deprotection of cyclopropane-1,1-dicarboxylic acid N-[4-[(7-benzyloxy-6-methoxyquinolin-4-yl)oxy]-3-fluorophenyl]amide N-(4-fluorophenyl)amide, which was prepared (48 %) from trifluoromethanesulfonic acid 7-benzyloxy-6-methoxyquinolin-4-yl ester and cyclopropane-1,1-dicarboxylic acid N-(3-fluoro-4-hydroxyphenyl)amide N-(4-fluorophenyl)amide, which was prepared (85 %) by deprotection of cyclopropane-1,1-dicarboxylic acid N-(4-benzyloxy-3-fluorophenyl)amide N-(4-fluorophenyl)amide, which was prepared (98 %) from (4-benzyloxy-3-fluorophenyl)amine and 1-(4-fluorophenylcarbamoyl)cyclopropanecarboxylic acid; addnl. details are given in the examples.

IT 64-04-0, Phenethylamine

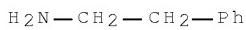
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of quinolines and quinazolines as inhibitors of c-Met and other

tyrosine kinases and therapeutic uses against proliferative diseases)

RN 64-04-0 HCAPLUS

CN Benzeneethanamine (CA INDEX NAME)



IC ICM A61K
 CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1, 27
 IT Antitumor agents
 Cytotoxic agents
 Human
 Neoplasm
 Structure-activity relationship
 (preparation of quinolines and quinazolines as inhibitors of c-Met and other tyrosine kinases and therapeutic uses against proliferative diseases)
 IT 849217-29-4P 849217-31-8P, N-[6-[(6,7-Dimethoxyquinolin-4-yl)oxy]-5-fluorobenzothiazol-2-yl]-2-phenylacetamide 849217-37-4P, 1-[3-Fluoro-4-[[6-methoxy-7-[(2-methyloctahydrocyclopenta[c]pyrrol-5-yl)methoxy]quinazolin-4-yl]oxy]phenyl]-3-(phenylacetyl)thiourea hydrochloride 849217-38-5P, 1-[3-Fluoro-4-[[6-methoxy-7-[(2-methyloctahydrocyclopenta[c]pyrrol-5-yl)methoxy]quinazolin-4-yl]oxy]phenyl]-3-(phenylacetyl)thiourea acetate 849217-41-0P 849217-42-1P 849217-43-2P 849217-44-3P 849217-52-3P, N-[4-[[7-[(2-(Diethylamino)ethyl)oxy]-6-(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849217-63-6P, N-[3-Fluoro-4-[[6-methoxy-7-[3-(morpholin-4-yl)propoxy]quinolin-4-yl]oxy]phenyl]-N'-(2-phenylethyl)ethanediamide 849217-64-7P, N-[3-Fluoro-4-[[6-(methyloxy)-7-[(3-(morpholin-4-yl)propyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849217-67-0P, N-[3-Fluoro-4-[[6-(methyloxy)-7-[(3-(morpholin-4-yl)propyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849217-68-1P 849217-72-7P, N-[3-Fluoro-4-[[6-(methyloxy)-7-[(1-methylpiperidin-4-yl)methyl]oxy]quinazolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide hydrochloride 849217-74-9P, N-[3-Fluoro-4-[[7-(methyloxy)-6-[(3-(morpholin-4-yl)propyl)oxy]quinazolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849217-76-1P, N-[3-Fluoro-4-[[7-(methyloxy)-6-[(1-methylpiperidin-4-yl)methyl]oxy]quinazolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849217-78-3P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-[(4-fluorophenyl)methyl]cyclopropane-1,1-dicarboxamide 849217-79-4P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-[2-(piperidin-1-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide 849217-80-7P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-[2-(pyrrololidin-1-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide 849217-81-8P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-[3-(morpholin-4-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide 849217-82-9P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-[2-(morpholin-4-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide 849217-83-0P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-[3-(piperidin-1-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide 849217-84-1P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-[3-(pyrrololidin-1-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide 849217-85-2P, N-[4-[[6,7-Bis(methyloxy)-2-(methylthio)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849217-90-9P, N-[4-[[2-Amino-6,7-bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide

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849217-94-3P, N-[3-Fluoro-4-[(2-(methylamino)-6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
849217-98-7P, N-[4-[[6-[[3-(Diethylamino)propyl]oxy]-7-(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849218-00-4P, N-(4-Fluorophenyl)-N'-[4-[(2-methyl-6,7-bis(methyloxy)quinazolin-4-yl]oxy]phenyl)cyclopropane-1,1-dicarboxamide
849218-06-0P, (1S*,2R*)-N-[3-Fluoro-4-[(6-(methyloxy)-7-[[3-(morpholin-4-yl)propyl]oxy]quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide hydrochloride 849218-12-8P
849218-13-9P, (2R*,3R*)-N-[3-Fluoro-4-[(6-(methyloxy)-7-[[3-(morpholin-4-yl)propyl]oxy]quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide 849218-20-8P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)azetidine-3,3-dicarboxamide 849218-21-9P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)azetidine-3,3-dicarboxamide acetate 849218-22-0P,
N-[3-Fluoro-4-[(6-(methyloxy)-7-[[1-methylpiperidin-4-yl]methyl]oxy]quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide hydrochloride 849218-25-3P 849218-26-4P
849218-27-5P, N-[4-[[7-[[2-(Diethylamino)ethyl]oxy]-6-(methyloxy)quinazolin-4-yl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)-2,2-dimethylcyclopropane-1,1-dicarboxamide 849218-29-7P 849218-30-0P
849218-32-2P, N-[3-Fluoro-4-[(6-(methyloxy)-7-[[3-(piperazin-1-yl)propyl]oxy]quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849218-33-3P,
N-[3-Fluoro-4-[(6-(methyloxy)-7-[[3-(piperazin-1-yl)propyl]oxy]quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide bis(trifluoroacetate) 849218-34-4P,
N-[[[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl](methyl)amino]carbonothioyl]-2-phenylacetamide
849218-35-5P, 1-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]imidazolidin-2-one 849218-36-6P,
1-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-3-(phenylmethyl)imidazolidin-2-one 849218-37-7P,
1-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-3-(phenylacetyl)imidazolidin-2-one 849218-38-8P, Ethyl 2-[[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]amino]-2-oxoacetate 849218-39-9P, N'-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N-methyl-N-(2-phenylethyl)sulfamide 849218-40-2P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-3-(phenylmethyl)-1,2,4-oxadiazol-5-amine 849218-41-3P,
1-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]piperidin-2-one 849218-42-4P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(phenylmethyl)ethanediamide 849218-43-5P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-4-phenyl-1,3-thiazol-2-amine 849218-44-6P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-1-phenylmethanesulfonamide 849218-45-7P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-2-phenylethanesulfonamide 849218-46-8P,
4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluoro-N-(phenylmethyl)benzenesulfonamide 849218-47-9P,
4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluoro-N-methyl-N-(phenylmethyl)benzenesulfonamide 849218-48-0P,
4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluoro-N-(2-phenylethyl)benzenesulfonamide 849218-49-1P,
4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluoro-N-methyl-N-(2-phenylethyl)benzenesulfonamide 849218-50-4P,
4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluoro-N-(3-phenylpropyl)benzenesulfonamide 849218-51-5P,
1-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]pyrrolidin-2-

one 849218-52-6P, 4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl (phenylmethyl)carbamate 849218-53-7P,
 4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl (2-phenylethyl)carbamate
 849218-54-8P, 4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluoro-N-methyl-N-(3-phenylpropyl)benzenesulfonamide 849218-55-9P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-phenylethanediamide 849218-56-0P,
 4-[[6,7-Bis(methyloxy)quinolin-4-yl]amino]-N-(3-phenylpropyl)benzamide
 849218-57-1P 849218-58-2P, 4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluoro-N-[2-(phenyloxy)ethyl]benzenesulfonamide 849218-59-3P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N-(3-phenylpropylsulfonyl)-3-phenylpropane-1-sulfonamide 849218-60-6P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-3-phenylpropane-1-sulfonamide 849218-61-7P,
 N'-[[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]sulfonyl]-N-phenylglycinamide 849218-62-8P, N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]pyridin-3-yl]-2-phenylacetamide 849218-63-9P,
 6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-1,3-benzothiazol-2-amine
 849218-64-0P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(2-(morpholin-4-yl)ethyl)ethanediamide 849218-65-1P,
 1,1-Dimethylethyl [2-[[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]amino]-2-oxoethyl](phenylmethyl)carbamate 849218-66-2P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(phenylmethyl)glycinamide 849218-67-3P,
 N'-Acetyl-N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(phenylmethyl)glycinamide 849218-68-4P,
 N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-1,3-benzothiazol-2-yl]-2-phenylacetamide 849218-69-5P, 1,1-Dimethylethyl
 [2-[[6-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]pyridin-3-yl]amino]-2-oxoethyl](phenylmethyl)carbamate 849218-70-8P,
 N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]pyridin-3-yl]-N'-(phenylmethyl)glycinamide 849218-71-9P,
 N'-Acetyl-N-[6-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]pyridin-3-yl]-N'-(phenylmethyl)glycinamide 849218-72-0P,
 N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]pyridin-3-yl]-3-phenylpropanamide 849218-73-1P, N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]pyridin-3-yl]-4-phenylbutanamide 849218-74-2P,
 N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]pyridin-3-yl]-N'-(phenylmethyl)glycinamide 849218-75-3P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(2-(4-(methyloxy)phenyl)ethyl)ethanediamide 849218-76-4P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(phenylmethyl)glycinamide 849218-77-5P,
 N-[[4-[[6,7-Bis(methyloxy)quinolin-4-yl]amino]phenyl]amino]carbonothioyl]-2-phenylacetamide 849218-78-6P, N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-fluoro-1,3-benzothiazol-2-yl]-3-phenylpropanamide 849218-79-7P
 , N-[[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]amino]carbonothioyl]-2-phenylacetamide 849218-80-0P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(2,3-dihydro-1H-inden-1-yl)ethanediamide 849218-81-1P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(2,3-dihydro-1H-inden-2-yl)ethanediamide 849218-82-2P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(1,2,3,4-tetrahydronaphthalen-1-yl)ethanediamide 849218-83-3P,
 N'-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N-(2-phenylethyl)-N-(phenylmethyl)sulfamide 849218-84-4P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(trifluoroacetyl)glycinamide 849218-85-5P,
 N-[2-[[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]amino]-2-oxoethyl]benzamide 849218-86-6P,

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N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]pyridin-3-yl]-N'-(4-fluorophenyl)propanediamide 849218-87-7P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(2S)-1,2,3,4-tetrahydronaphthalen-2-yl)ethanediame 849218-88-8P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-[2-(4-methylphenyl)ethyl]ethanediame 849218-89-9P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(2-phenylpropyl)ethanediame 849218-90-2P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-[2-(4-chlorophenyl)ethyl]ethanediame 849218-91-3P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N,N'-bis(phenylmethyl)sulfamide 849218-92-4P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N,N'-bis(2-phenylethyl)sulfamide 849218-93-5P, Ethyl
2-[[6-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]amino]-2-oxoacetate 849218-94-6P, N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]-N'-(2-phenylethyl)ethanediame 849218-95-7P,
N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]-N'-(4-fluorophenyl)propanediamide 849218-96-8P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(2R)-1,2,3,4-tetrahydronaphthalen-2-yl)ethanediame 849218-97-9P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-[2-(1-methylpyrrolidin-2-yl)ethyl]ethanediame 849218-98-0P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-[2-(phenyloxy)ethyl]ethanediame 849218-99-1P,
1-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-3-[2-hydroxy-1-(phenylmethyl)ethyl]urea 849219-00-7P,
1-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-3-[(4-methylphenyl)sulfonyl]-4-(phenylmethyl)imidazolidin-2-one 849219-01-8P,
N'-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N-methyl-N-(2-phenylethyl)ethanediame 849219-02-9P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-[3-(trifluoromethyl)phenyl]methylethanediame 849219-03-0P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-[2-[3-(trifluoromethyl)phenyl]ethyl]ethanediame 849219-04-1P,
N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]-3-oxo-4-phenylbutanamide 849219-05-2P, N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]-2-[3-(trifluoromethyl)phenyl]acetamide 849219-06-3P, 6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-fluoro-N-[2-(phenyloxy)ethyl]-1,3-benzothiazol-2-amine 849219-07-4P,
6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-fluoro-N-[2-(piperidin-1-yl)ethyl]-1,3-benzothiazol-2-amine 849219-08-5P,
6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-fluoro-N-methyl-N-(2-phenylethyl)-1,3-benzothiazol-2-amine 849219-09-6P,
6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-fluoro-N-[2-(pyrrolidin-1-yl)ethyl]-1,3-benzothiazol-2-amine 849219-10-9P,
6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-fluoro-N-[3-(trifluoromethyl)phenyl]methylethanediame 849219-11-0P,
6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-fluoro-N-[2-[3-(trifluoromethyl)phenyl]ethyl]-1,3-benzothiazol-2-amine 849219-12-1P,
N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]-N'-[3-(trifluoromethyl)phenyl]propanediamide 849219-13-2P,
N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-fluoro-1,3-benzothiazol-2-yl]-2-[3-(trifluoromethyl)phenyl]acetamide 849219-14-3P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-[3-(trifluoromethyl)phenyl]glycinamide 849219-15-4P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(2-phenylethyl)glycinamide 849219-16-5P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-[2-[3-(trifluoromethyl)phenyl]ethyl]glycinamide 849219-17-6P,

1,1-Dimethylethyl [2-[[6-[6,7-bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]amino]-2-oxoethyl](phenylmethyl)carbamate
 849219-18-7P, N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]-N'-(phenylmethyl)glycinamide 849219-19-8P,
 N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-fluoro-1,3-benzothiazol-2-yl]-2-[3,5-bis(trifluoromethyl)phenyl]acetamide 849219-20-1P,
 N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-fluoro-1,3-benzothiazol-2-yl]-2-[2-chloro-5-(trifluoromethyl)phenyl]acetamide 849219-21-2P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(1,2,3,4-tetrahydroisoquinolin-1-ylmethyl)ethanediame 849219-22-3P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(2-methyl-1,2,3,4-tetrahydroisoquinolin-1-yl)methylethanediame 849219-23-4P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(methyl-N'-[[3-(trifluoromethyl)phenyl]methyl]glycinamide 849219-24-5P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(methyl-N'-[2-[3-(trifluoromethyl)phenyl]ethyl]glycinamide 849219-25-6P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(methyl-N'-(2-phenylethyl)glycinamide 849219-26-7P,
 1-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-4-(phenylmethyl)imidazolidin-2-one 849219-27-8P,
 N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]pyridazin-3-yl]-N'-(4-fluorophenyl)propanediame 849219-28-9P,
 N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]-N'-(2-chlorophenyl)propanediame 849219-29-0P,
 N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]-N'-(3-chlorophenyl)propanediame 849219-30-3P,
 N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]-N'-(methyl-N'-(phenylmethyl)glycinamide 849219-31-4P,
 N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]-N'-(4-chlorophenyl)propanediame 849219-32-5P,
 (2E)-N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-2-[(methyloxy)imino]propanamide 849219-33-6P,
 (2E)-N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-2-[(ethyloxy)imino]propanamide 849219-34-7P,
 (2E)-N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-2-[(phenylmethyl)oxy]imino]propanamide 849219-35-8P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-1-(phenylmethyl)prolinamide 849219-36-9P,
 1-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-3-[(4-methylphenyl)sulfonyl]-4-(phenylmethyl)imidazolidin-2-one 849219-37-0P,
 1-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-4-(phenylmethyl)imidazolidin-2-one 849219-38-1P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-4-(phenylmethyl)-4,5-dihydro-1,3-oxazol-2-amine 849219-39-2P,
 6,7-Bis(methyloxy)-4-[[4-[(phenylmethyl)piperazin-1-yl]phenyl]oxy]quinoline 849219-40-5P,
 1-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-4-(phenylmethyl)piperazin-2-one 849219-41-6P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(phenylmethyl)alaninamide 849219-42-7P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(methyl-N'-(phenylmethyl)alaninamide 849219-43-8P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(phenylmethyl)leucinamide 849219-44-9P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(methyl-N'-(phenylmethyl)leucinamide 849219-45-0P,
 N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(phenylmethyl)valinamide 849219-47-2P,
 N-[5-Chloro-6-[[6-(methyloxy)-4-(piperidin-4-ylmethyl)oxy]quinolin-7-yl]oxy]pyridin-3-yl]-N'-(4-fluorophenyl)propanediame 849219-48-3P,

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1-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-4-(phenylmethyl)tetrahydropyrimidin-2(1H)-one 849219-49-4P,
N-[3-Fluoro-4-[[6-(methyloxy)-7-[(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-(2-phenylethyl)ethanediame 849219-50-7P,
N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849219-51-8P,
N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]-N'-(4-fluorophenyl)cyclobutane-1,1-dicarboxamide 849219-52-9P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-methyl-N'-(phenylmethyl)valinamide 849219-53-0P,
(2E)-N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-2-[(phenyloxy)imino]propanamide 849219-54-1P,
(2E)-N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]phenyl]-2-phenyl-2-[(phenylmethyl)oxy]iminoethanamide 849219-55-2P,
6,7-Bis(methyloxy)-4-[[4-[4-(phenylmethyl)piperidin-1-yl]phenyl]oxy]quinoline 849219-56-3P,
N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-[2-(1-methylethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl]methylethanediame 849219-57-4P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(2-ethyl-1,2,3,4-tetrahydroisoquinolin-1-yl)methylethanediame 849219-58-5P, 1,1-Dimethylethyl 4-[[[4-[[3-chloro-5-[[3-[(4-fluorophenyl)amino]-3-oxoprop酰]amino]pyridin-2-yl]oxy]-6-(methyloxy)quinolin-7-yl]oxy]methyl]piperidine-1-carboxylate 849219-59-6P, N-[5-Chloro-6-[[6-(methyloxy)-7-[(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]pyridin-3-yl]-N'-(4-fluorophenyl)propanediame 849219-60-9P,
N-[5-Chloro-6-[[6-(methyloxy)-7-[(1-methylpiperidin-4-yl)methyl]oxy]quinolin-4-yl]oxy]pyridin-3-yl]-N'-(4-fluorophenyl)propanediame 849219-61-0P,
N-[4-[[7-[[3-(Diethylamino)propyl]oxy]-6-(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(2-phenylethyl)ethanediame 849219-62-1P
, N-[3-Fluoro-4-[[6-(methyloxy)-7-[[3-(piperidin-1-yl)propyl]oxy]quinolin-4-yl]oxy]phenyl]-N'-(2-phenylethyl)ethanediame 849219-63-2P,
N-[4-[[7-[[2-(Diethylamino)ethyl]oxy]-6-(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(2-phenylethyl)ethanediame 849219-64-3P,
N'-[3-Fluoro-4-[[6-(methyloxy)-7-[[1-methylpiperidin-4-yl]methyl]oxy]quinolin-4-yl]oxy]phenyl]-N-methyl-N-(2-phenylethyl)ethanediame 849219-65-4P 849219-66-5P,
2-(3,4-Dihydroisoquinolin-2(1H)-yl)-N-[3-fluoro-4-[[6-(methyloxy)-7-[(1-methylpiperidin-4-yl)methyl]oxy]quinolin-4-yl]oxy]phenyl]-2-(oxo)acetamide 849219-67-6P, N-[3-Fluoro-4-[[6-(methyloxy)-7-[(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-2-oxo-2-(3-phenylpyrrolidin-1-yl)acetamide 849219-68-7P, N-[3-Fluoro-4-[[6-(methyloxy)-7-[(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-2-oxo-2-(2-phenylmorpholin-4-yl)acetamide 849219-69-8P, N-[2-(Dimethylamino)-2-phenylethyl]-N'-[3-fluoro-4-[[6-(methyloxy)-7-[(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]ethanediame 849219-70-1P,
N-[3-Fluoro-4-[[6-(methyloxy)-7-[(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-(2-oxo-2-phenylethyl)ethanediame 849219-71-2P,
N-[6-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-chloropyridin-3-yl]-2,2-difluoro-N'-(4-fluorophenyl)propanediame 849219-72-3P,
N-[3-Fluoro-4-[[6-(methyloxy)-7-[[1-methylpiperidin-4-yl]methyl]oxy]quinolin-4-yl]oxy]phenyl]-N'-(phenylmethyl)ethanediame 849219-73-4P, N-[3-Fluoro-4-[[6-(methyloxy)-7-[(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-[2-(2-phenylethyl)ethyl]ethanediame 849219-74-5P,
N-[2-(3-Chlorophenyl)ethyl]-N'-[3-fluoro-4-[[6-(methyloxy)-7-[(piperidin-4-yl)methyl]oxy]quinolin-4-yl]oxy]ethanediame 849219-75-6P,
N-[3-Fluoro-4-[[6-(methyloxy)-7-[(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-[2-[2-(methyloxy)phenyl]ethyl]ethanediame

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849219-76-7P, N-[3-Fluoro-4-[(6-(methyloxy)-7-(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-(2-(pyridin-3-yl)ethyl)ethanediamide 849219-77-8P,
N-[3-Fluoro-4-[(6-(methyloxy)-7-(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-(phenylmethyl)ethanediamide 849219-78-9P,
N-[2-[2,5-Bis(methyloxy)phenyl]ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl)ethanediamide
849219-79-0P, N-[3-Fluoro-4-[(6-(methyloxy)-7-(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-(2-[2-(trifluoromethyl)phenyl]ethyl)ethanediamide 849219-80-3P,
N-[2-[2-(Ethyloxy)phenyl]ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy)phenyl)ethanediamide
849219-81-4P, N-[2-(2,4-Dimethylphenyl)ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-[(piperidin-4-yl)methyl]oxy]quinolin-4-yl]oxy)phenyl)ethanediamide 849219-82-5P,
N-[3-Fluoro-4-[(6-(methyloxy)-7-(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-(1S)-2-(4-methylphenyl)-1-phenylethyl)ethanediamide
849219-83-6P, N-[2-(4-Chlorophenyl)ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-[(piperidin-4-yl)methyl]oxy]quinolin-4-yl]oxy)phenyl)ethanediamide
849219-84-7P, [(3-Fluoro-4-[(6-(methyloxy)-7-[(1-methylpiperidin-4-yl)methyl]oxy]quinolin-4-yl]oxy)phenyl]amino](oxo)acetic acid
849219-85-8P, N-[3-Fluoro-4-[(6-(methyloxy)-7-(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-(2-(3-fluorophenyl)ethyl)ethanediamide 849219-86-9P,
N-[2-(2-Chlorophenyl)ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-[(piperidin-4-yl)methyl]oxy]quinolin-4-yl]oxy)phenyl)ethanediamide 849219-87-0P,
N-[3-Fluoro-4-[(6-(methyloxy)-7-(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-(2-[3-(methyloxy)phenyl]ethyl)ethanediamide
849219-88-1P, N-(1,2-Diphenylethyl)-N'-(3-fluoro-4-[(6-(methyloxy)-7-[(piperidin-4-yl)methyl]oxy]quinolin-4-yl]oxy)phenyl)ethanediamide
849219-89-2P, N-[2-(2,4-Dichlorophenyl)ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-[(piperidin-4-yl)methyl]oxy]quinolin-4-yl]oxy)phenyl)ethanediamide 849219-90-5P,
N-[2-[3,4-Bis(methyloxy)phenyl]ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy)phenyl)ethanediamide
849219-91-6P, N-[2-(4-Ethylphenyl)ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-[(piperidin-4-yl)methyl]oxy]quinolin-4-yl]oxy)phenyl)ethanediamide
849219-92-7P, N-[2-[4-(Ethyloxy)phenyl]ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-[(piperidin-4-yl)methyl]oxy]quinolin-4-yl]oxy)phenyl)ethanediamide 849219-93-8P,
N-[2-[4-(Ethyloxy)-3-(methyloxy)phenyl]ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-[(piperidin-4-yl)methyl]oxy]quinolin-4-yl]oxy)phenyl)ethanediamide 849219-94-9P,
N-[3-Fluoro-4-[(6-(methyloxy)-7-(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-(2-[4-(phenyloxy)phenyl]ethyl)ethanediamide
849219-95-0P, N-[2-[3-(Ethyloxy)-4-(methyloxy)phenyl]ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy)phenyl)ethanediamide 849219-96-1P,
N-[3-Fluoro-4-[(6-(methyloxy)-7-(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-(2-(pyridin-2-yl)ethyl)ethanediamide 849219-97-2P,
N-[3-Fluoro-4-[(6-(methyloxy)-7-(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-(2-(pyridin-4-yl)ethyl)ethanediamide 849219-98-3P,
N-[3-Fluoro-4-[(6-(methyloxy)-7-(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-(2-(4-fluorophenyl)ethyl)ethanediamide 849219-99-4P,
N-[2-(2-Bromophenyl)ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-[(piperidin-4-yl)methyl]oxy]quinolin-4-yl]oxy)phenyl)ethanediamide 849220-00-4P,
N-[2-(2-Chloro-6-fluorophenyl)ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-[(piperidin-4-yl)methyl]oxy]quinolin-4-yl]oxy)phenyl)ethanediamide
849220-01-5P, N-[3-Fluoro-4-[(6-(methyloxy)-7-(piperidin-4-ylmethyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-(2R)-2-

phenylpropyl)ethanediamide 849220-02-6P,
 N-(2,3-Dihydro-1H-inden-1-yl)-N'-(3-fluoro-4-[(6-(methyloxy)-7-
 [(piperidin-4-yl)methyl]oxy]quinolin-4-yl)oxy]phenyl)ethanediamide
 849220-03-7P, N-[3-Fluoro-4-[(6-(methyloxy)-7-[(1-methylpiperidin-4-
 yl)methyl]oxy]quinolin-4-yl]oxy]phenyl)-N'-(2-methylpropyl)ethanediamide
 849220-04-8P, N-[3-Fluoro-4-[(6-(methyloxy)-7-[(1-methylpiperidin-4-
 yl)methyl]oxy]quinolin-4-yl]oxy]phenyl)-N'-(3-methylbutyl)ethanediamide
 849220-05-9P, N-[3-Fluoro-4-[(6-(methyloxy)-7-[(1-methylpiperidin-4-
 yl)methyl]oxy]quinolin-4-yl]oxy]phenyl)-N'-(2R)-2-
 phenylpropyl)ethanediamide 849220-06-0P,
 N-[3-Fluoro-4-[(6-(methyloxy)-7-[(1-methylpiperidin-4-
 yl)methyl]oxy]quinolin-4-yl]oxy]phenyl)-N'-(2-phenylpropyl)ethanediamide
 849220-07-1P, N-(2,3-Dihydro-1H-inden-2-yl)-N'-(3-fluoro-4-[(6-(methyloxy)-
 7-[(1-methylpiperidin-4-yl)methyl]oxy]quinolin-4-
 yl)oxy]phenyl)ethanediamide 849220-08-2P,
 N-[3-Fluoro-4-[(6-(methyloxy)-7-[(piperidin-4-ylmethyl)oxy]quinolin-4-
 yl)oxy]phenyl)-N'-(1R)-1-phenylethyl)ethanediamide 849220-09-3P,
 N-[3-Fluoro-4-[(6-(methyloxy)-7-[(piperidin-4-ylmethyl)oxy]quinolin-4-
 yl)oxy]phenyl)-N'-(1S)-1-phenylethyl)ethanediamide 849220-10-6P,
 N-[2-(3-Bromophenyl)ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-[(piperidin-4-
 yl)methyl]oxy]quinolin-4-yl)oxy]phenyl)ethanediamide 849220-11-7P,
 N-[2-(2,6-Dichlorophenyl)ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-
 [(piperidin-4-yl)methyl]oxy]quinolin-4-yl)oxy]phenyl)ethanediamide
 849220-12-8P, N-[2-(1,3-Benzodioxol-5-yl)ethyl]-N'-(3-fluoro-4-[(6-
 (methyloxy)-7-[(piperidin-4-yl)methyl]oxy]quinolin-4-
 yl)oxy]phenyl)ethanediamide 849220-13-9P,
 N-[5-Chloro-6-[(6-(methyloxy)-7-[(1-methylpiperidin-4-
 yl)methyl]oxy]quinolin-4-yl]oxy]pyridin-3-yl)-N'-(4-
 fluorophenyl)cyclopropane-1,1-dicarboxamide 849220-14-0P,
 N-[2-[3-Bromo-4-(methyloxy)phenyl]ethyl]-N'-(3-fluoro-4-[(6-(methyloxy)-7-
 [(piperidin-4-ylmethyl)oxy]quinolin-4-yl)oxy]phenyl)ethanediamide
 849220-15-1P, N-[2-[3,5-Bis(methyloxy)phenyl]ethyl]-N'-(3-fluoro-4-[(6-
 (methyloxy)-7-[(piperidin-4-ylmethyl)oxy]quinolin-4-
 yl)oxy]phenyl)ethanediamide
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(drug candidate; preparation of quinolines and quinazolines as inhibitors

of

c-Met and other tyrosine kinases and therapeutic uses against
 proliferative diseases)

IT 62-53-3, Phenylamine, reactions 64-04-0, Phenethylamine
 86-99-7, 7-Chloro-4-hydroxyquinoline 100-02-7, 4-Nitrophenol, reactions
 100-37-8, 2-(Diethylamino)ethanol 100-39-0, Benzyl bromide 100-46-9,
 Benzylamine, reactions 100-51-6, Benzyl alcohol, reactions 103-80-0,
 Phenylacetyl chloride 106-89-8, Epichlorohydrin, reactions 109-94-4,
 Ethyl formate 123-30-8, 4-Aminophenol 140-75-0, 4-Fluorobenzylamine
 369-34-6, 1,2-Difluoro-4-nitrobenzene 369-35-7,
 (2-Fluoro-4-nitrophenyl)amine 371-40-4, 4-Fluoroaniline 399-96-2,
 4-Amino-2-fluorophenol 403-19-0, 2-Fluoro-4-nitrophenol 498-02-2
 598-10-7, 1,1-Cyclopropanedicarboxylic acid 622-93-5,
 N-(3-Hydroxypropyl)diethylamine 869-24-9, N-(2-Chloroethyl)diethylamine
 hydrochloride 2133-40-6 4441-30-9, 4-(3-Hydroxypropyl)morpholine
 4548-45-2, 2-Chloro-5-nitropyridine 4755-77-5, Ethyl oxalyl chloride
 5445-51-2, 1,1-Cyclobutanedicarboxylic acid 6315-89-5,
 3,4-Dimethoxyaniline 6941-54-4 13425-93-9, 6,7-Dimethoxyquinolin-4-ol
 13790-39-1, 4-Chloro-6,7-dimethoxyquinazoline 16684-31-4 18162-48-6,
 tert-Butyldimethylsilyl chloride 18600-42-5, 4-Nitrobenzylamine
 hydrochloride 19577-83-4 20691-89-8 23356-96-9, (S)-(+) -Prolinol
 26759-46-6, 2-Amino-4,5-dimethoxybenzoic acid methyl ester 29313-32-4,

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Phenylacetyl isothiocyanate 51388-20-6, 4-Benzylxyloxyaniline hydrochloride
 55727-59-8 57616-74-7, N-(3-Chloropropyl)morpholine hydrochloride
 68832-13-3 76211-05-7, Ethyl octahydro-2H-quinolizine-3-carboxylate
 93138-55-7 95539-61-0 99380-85-5, ((4R)-1,3-Thiazolidin-4-yl)methanol
 100981-05-3, 5-[Bis(methylsulfanyl)methylene]-2,2-dimethyl-[1,3]dioxane-
 4,6-dione 106014-87-3, 1-Benzylazetidine-3,3-dicarboxylic acid
 112018-06-1 123207-48-7 127285-54-5, 6,7-Dimethoxy-1H-quinolin-4-one
 139228-12-9 141899-49-2 146231-54-1 157904-95-5 161975-39-9
 179688-01-8, 7-Benzylxyloxy-6-methoxy-3H-quinazolin-4-one 183365-31-3
 190728-25-7, [4-[(6,7-Dimethoxyquinolin-4-yl)oxy]phenyl]amine
 205448-29-9, 7-Benzylxyloxy-6-methoxy-1H-quinolin-4-one 211053-49-5,
 ((3R)-Morpholin-3-yl)methanol 286371-49-1 347161-74-4,
 [4-[(6,7-Dimethoxyquinolin-4-yl)oxy]-3-fluorophenyl]amine 479690-04-5
 650577-55-2 650578-72-6, 1,1-Dimethylethyl
 (3-endo)-3-(2-hydroxyethyl)-8-azabicyclo[3.2.1]octane-8-carboxylate
 767587-88-2 849217-25-0, 5-
 [(Methylsulfonyl)oxy]methyl]hexahydrocyclopenta[c]pyrrole-2-carboxylic
 acid benzyl ester 849217-33-0, 5-[(4-Chloro-6-methoxyquinazolin-7-
 yl)oxy]methyl]hexahydrocyclopenta[c]pyrrole-2-carboxylic acid benzyl ester
 849217-75-0, Cyclopropane-1,1-dicarboxylic acid
 N-[3-fluoro-4-[(6-hydroxy-7-methoxyquinazolin-4-yl)oxy]phenyl]amide
 N-(4-fluorophenyl)amide 849218-14-0,
 trans-2,3-Dimethylcyclopropane-1,1-dicarboxylic acid diethyl ester
 849218-24-2, Cyclopropane-1,1-dicarboxylic acid
 N-[3-fluoro-4-[(6-methoxy-7-(piperidin-4-ylmethoxy)quinolin-4-
 yl)oxy]phenyl]amide N-(4-fluorophenyl)amide trifluoroacetate
 849218-28-6, 2,2-Dimethylcyclopropane-1,1-dicarboxylic acid
 N-[3-fluoro-4-[(7-hydroxy-6-methoxyquinazolin-4-yl)oxy]phenyl]amide
 N-(4-fluorophenyl)amide 849482-10-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of quinolines and quinazolines as inhibitors of c-Met and
 other

tyrosine kinases and therapeutic uses against proliferative diseases)

L35 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:140787 HCAPLUS Full-text
 DOCUMENT NUMBER: 142:240718
 TITLE: Preparation of peptides for treating tumors
 INVENTOR(S): Zask, Arie; Kaplan, Joshua; Yamashita, Ayako; Niu,
 Chuan S.; Birnberg, Gary Harold; Norton, Emily;
 Cheung, Kinwang; Suayan, Ronald; Sandanayaka, Vincent;
 Hamann, Philip Ross; Ayral-Kaloustian, Semiramis
 PATENT ASSIGNEE(S): Wyeth Holdings Corporation, USA
 SOURCE: U.S. Pat. Appl. Publ., 64 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050037977	A1	20050217	US 2004-911300	20040804
US 7390910	B2	20080624		
WO 2005016958	A2	20050224	WO 2004-US25246	20040805
WO 2005016958	A3	20050602		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,				

10/666722

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
 SN, TD, TG

US 20080221181 A1 20080911 US 2008-104921 20080417
 PRIORITY APPLN. INFO.: US 2003-493841P P 20030808
 US 2004-911300 A3 20040804

OTHER SOURCE(S): CASREACT 142:240718; MARPAT 142:240718

AB The invention provides peptides A-CH(E)C(:B')NR6CHR7CONR8R9 [A is (un)substituted alkyl, alkenyl, aryl or cyclic hydrocarbyl or aza/oxa/thia analogs; B' is O or H₂; E is (un)substituted alkyl, aryl, cyclic hydrocarbyl, etc.; R₆-R₈ are H or groups defined by A; R₉ is an alkyl group which is substituted by sulfonyl, phosphoryl, acyl, hydroxyalkyl, etc.] which exhibit anticancer activity. Thus, N,β,β,3-tetramethyl-L-phenylalanyl-N1-[(1S,2E)-1-isopropyl-3-methyl-4-morpholino-4-oxobut-2-enyl]-N1,3-dimethyl-L-valinamide was prepared and showed IC₅₀ values 19.5, 56 and 1514 nM against KB, KB85 and KBV1 cell lines and 79% inhibition of tubulin polymerization at 0.3 μN.

IT 228266-40-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

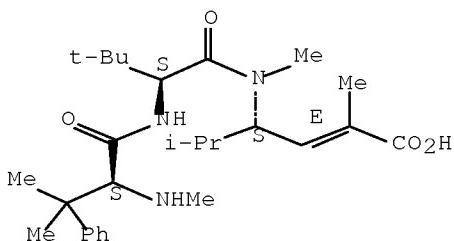
(preparation of peptides for treating tumors)

RN 228266-40-8 HCPLUS

CN L-Valinamide, N,β,β-trimethyl-L-phenylalanyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-buten-1-yl]-N,3-dimethyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.

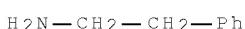


IT 64-04-0, Phenethylamine 156-06-9, 3-Phenyl 2
 oxopropanoic acid 2280-27-5 5717-37-3,
 Carbethoxyethylidene triphenylphosphorane 138802-17-2
 228266-38-4 500229-47-0 610786-70-4
 676631-65-5 676631-81-5 676631-97-3
 676632-00-1 676632-05-6 676632-08-9
 676633-60-6

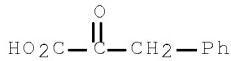
RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of peptides for treating tumors)

RN 64-04-0 HCPLUS

CN Benzeneethanamine (CA INDEX NAME)

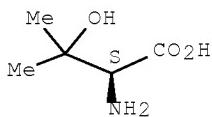


RN 156-06-9 HCAPLUS
CN Benzenepropanoic acid, α -oxo- (CA INDEX NAME)



RN 2280-27-5 HCAPLUS
CN L-Threonine, 3-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

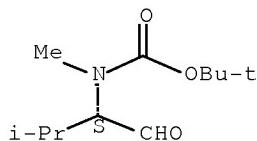


RN 5717-37-3 HCAPLUS
CN Propanoic acid, 2-(triphenylphosphoranylidene)-, ethyl ester (CA INDEX NAME)



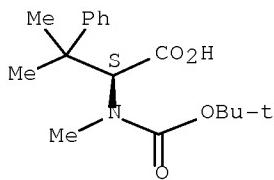
RN 138802-17-2 HCAPLUS
CN Carbamic acid, [(1S)-1-formyl-2-methylpropyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 228266-38-4 HCAPLUS
CN L-Phenylalanine, N-[(1,1-dimethylethoxy)carbonyl]- α , β -trimethyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

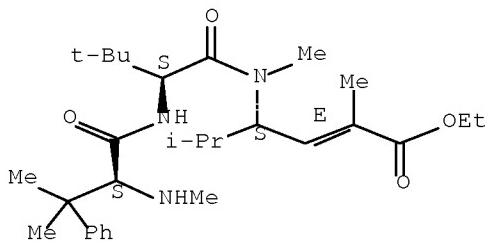


RN 500229-47-0 HCPLUS

CN L-Valinamide, N,β,β-trimethyl-L-phenylalanyl-N-[(1S,2E)-4-ethoxy-3-methyl-1-(1-methylethyl)-4-oxo-2-but enyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

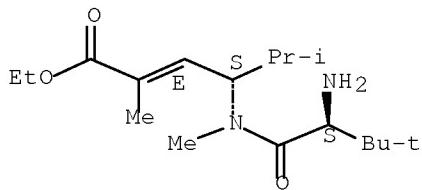


RN 610786-70-4 HCPLUS

CN 2-Hexenoic acid, 4-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]methylamino]-2,5-dimethyl-, ethyl ester, hydrochloride (1:1), (2E,4S)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



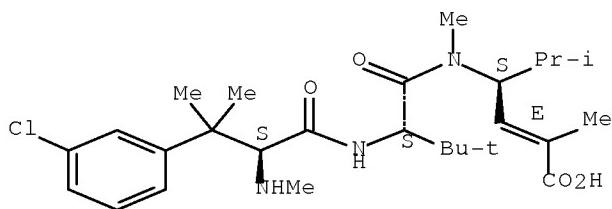
● HCl

RN 676631-65-5 HCPLUS

CN L-Valinamide, 3-chloro-N,β,β-trimethyl-L-phenylalanyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-but enyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

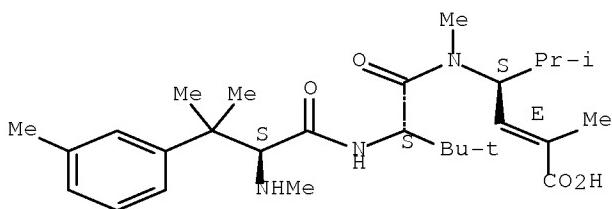


RN 676631-81-5 HCPLUS

CN L-Valinamide, N,β,β,3-tetramethyl-L-phenylalanyl-N-[(1S, 2E)-3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

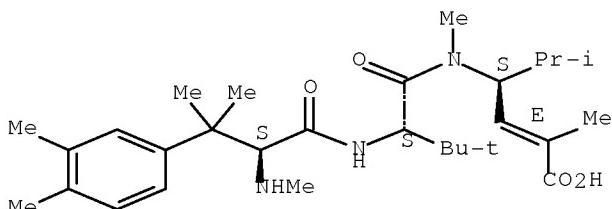


RN 676631-97-3 HCPLUS

CN L-Valinamide, N,β,β,3,4-pentamethyl-L-phenylalanyl-N-[(1S, 2E)-3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

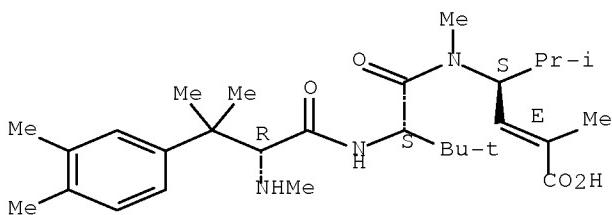


RN 676632-00-1 HCPLUS

CN L-Valinamide, N,β,β,3,4-pentamethyl-D-phenylalanyl-N-[(1S, 2E)-3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

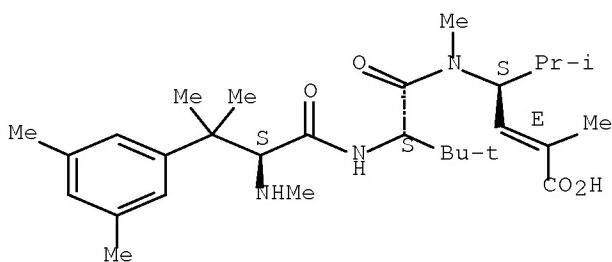


RN 676632-05-6 HCPLUS

CN L-Valinamide, N,β,β,3,5-pentamethyl-L-phenylalanyl-N-[(1S, 2E)-3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

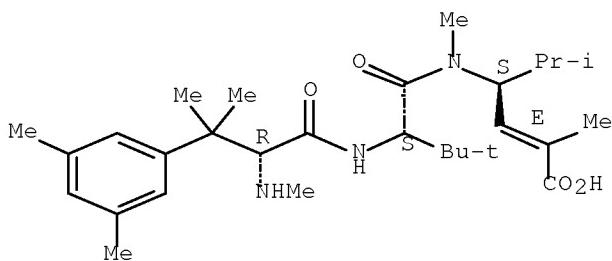


RN 676632-08-9 HCPLUS

CN L-Valinamide, N,β,β,3,5-pentamethyl-D-phenylalanyl-N-[(1S, 2E)-3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

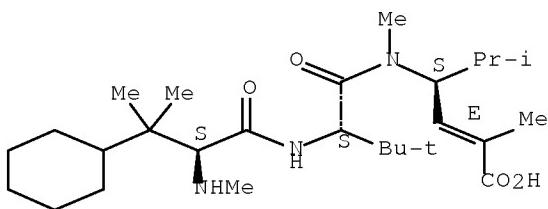


RN 676633-60-6 HCPLUS

CN L-Valinamide, 3-cyclohexyl-N-methyl-L-valyl-N-[(1S, 2E)-3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

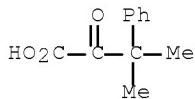


IT 91133-59-4P 676629-67-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptides for treating tumors)

RN 91133-59-4 HCPLUS

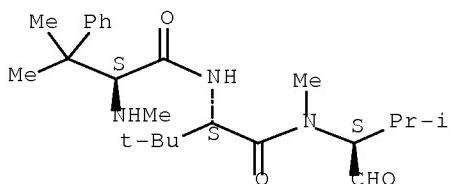
CN Benzene propanoic acid, β,β -dimethyl- α -oxo- (CA INDEX NAME)



RN 676629-67-7 HCPLUS

CN L-Valinamide, N, β,β -trimethyl-L-phenylalanyl-N-[(1S)-1-formyl-2-methylpropyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K038-04

ICS A61K031-277

INCL 514019000; 514513000; 514528000; 514616000; 558410000; 558254000;
564152000; 564154000

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

IT Structure-activity relationship

(antitumor; preparation of peptides for treating tumors)

IT Antitumor agents

Neoplasm

(preparation of peptides for treating tumors)

IT Peptides, preparation

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

10/666722

	(Preparation); RACT (Reactant or reagent); USES (Uses) (preparation of peptides for treating tumors)				
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	845292-17-3P	845292-20-8P	845292-23-1P	845292-32-2P	845292-33-3P
	845292-35-5P	845292-36-6P	845292-37-7P	845292-38-8P	845292-39-9P
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	RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (preparation of peptides for treating tumors)				
IT	228266-40-8P	610786-90-8P	610787-28-5P	755757-91-6P	
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	873530-02-0P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of peptides for treating tumors)				
IT	64-04-0, Phenethylamine 100-58-3, Phenylmagnesium bromide 103-82-2, Benzeneacetic acid, reactions 106-93-4, 1 2 Dibromoethane 109-01-3, 1 Methylpiperazine 110-91-8, Morpholine, reactions 156-06-9, 3-Phenyl 2 oxopropanoic acid 288-47-1, Thiazole 475-11-6, n Methyl L-proline 515-40-2, Neophyl chloride 529-34-0, α-Tetralone 556-56-9, Allyl iodide 616-04-6, 1-Methylhydantoin 624-92-0, Dimethyldisulfide 712-76-5, 4-Phenylbenzylamine 836-43-1, 4 Benzylxy benzyl alcohol 877-96-3 1779-28-8 2133-40-6 2280-27-5 2759-28-6, 1 Benzylpiperazine 2942-58-7, Diethyl cyanophosphonate 2999-46-4, Ethyl isocyanoacetate 3034-53-5, 2 Bromothiazole 5717-37-3, Carbethoxyethylidene triphenylphosphorane 15761-39-4 16001-93-7, Tetramethyl methylenediphosphonate 16640-68-9, Triphenylphosphoranylidene acetonitrile 17016-83-0, s 4 Isopropyl 2 oxazolidinone 18650-39-0				

10/666722

36982-84-0, Trisyl azide 40216-83-9 45170-31-8 51154-06-4
 62965-35-9 65365-28-8 68641-49-6, Bis(2-oxo-3-oxazolidinyl)phosphinic chloride 69610-41-9, Boc prolinal 73300-75-1 77877-20-4 82650-30-4
 90719-32-7 95378-36-2 138802-17-2 150019-50-4 165534-43-0,
 Depbt 169870-82-0 184434-17-1 187345-38-6 228266-38-4
 500229-47-0 610786-70-4 676631-65-5
 676631-81-5 676631-97-3 676632-00-1
 676632-05-6 676632-08-9 676633-60-6
 765932-28-3 845293-04-1 845293-06-3 845293-09-6 845293-36-9
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of peptides for treating tumors)

IT 1010-48-6P 67319-04-4P, 1-Ethoxymethyl-1H-imidazole 74641-60-4P, n
 Methylphenylglycine 74844-93-2P 77586-77-7P 77586-78-8P
 91133-59-4P 92235-33-1P 95092-10-7P 109133-93-9P
 120205-50-7P 120205-54-1P 130199-65-4P, 2 Thiazolemethanamine, α phenylmethyl, s 133120-91-9P 133565-38-5P 133645-51-9P
 140670-72-0P 144774-99-2P 144775-06-4P 144831-03-8P, 2
 Thiazolemethanol, α phenylmethyl, r 149606-89-3P 159525-39-0P
 169768-92-7P 169768-95-0P 179039-97-5P 180715-99-5P 182573-17-7P
 186145-08-4P 228266-34-0P 676629-67-7P 765930-74-3P
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 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of peptides for treating tumors)

IT 765931-16-6P 765932-37-4P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of peptides for treating tumors)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 4 OF 4 HCPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:1154654 HCPLUS Full-text
 DOCUMENT NUMBER: 142:93182
 TITLE: Preparation of compounds for treating amyloid-related diseases
 INVENTOR(S): Kong, Xianqi; Migneault, David; Valade, Isabelle; Wu, Xinfu; Gervais, Francine
 PATENT ASSIGNEE(S): Neurochem International Limited, Switz.
 SOURCE: PCT Int. Appl., 243 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 13
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004113275	A2	20041229	WO 2004-IB2375	20040621
WO 2004113275	A3	20051027		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,				

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NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20050038117	A1	20050217	US 2004-871365	20040618
US 7244764	B2	20070717		
US 7414076	B2	20080819	US 2004-871514	20040618
US 20050096385	A1	20050505		
AU 2004249529	A1	20041229	AU 2004-249529	20040621
CA 2529257	A1	20041229	CA 2004-2529257	20040621
EP 1644325	A2	20060412	EP 2004-744034	20040621
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004011743	A	20060808	BR 2004-11743	20040621
CN 1839118	A	20060927	CN 2004-80024207	20040621
JP 2007516939	T	20070628	JP 2006-516599	20040621
NO 2005005894	A	20060321	NO 2005-5894	20051212
MX 2005014166	A	20060313	MX 2005-14166	20051221
KR 2006023172	A	20060313	KR 2005-724647	20051222
IN 2006CN00242	A	20070518	IN 2006-CN242	20060119
US 20080015180	A1	20080117	US 2007-807759	20070530
PRIORITY APPLN. INFO.:				
			US 2003-480906P	P 20030623
			US 2003-512047P	P 20031017
			US 2004-871365	A 20040618
			US 2004-871514	A 20040618
			WO 2004-IB2375	W 20040621

OTHER SOURCE(S): CASREACT 142:93182; MARPAT 142:93182

AB Methods for preparing a variety of compds. R1L1N(R2)L2Y [R1 = (aryl)cycloalkyl, heterocyclyl, aryl, C2-C10 alkyl, bicyclic or tricyclic ring, fused bicyclic or tricyclic; R2 = H, alkyl; Y = SO₃-X+, X+ = H, cation; L1, L2 = independently C1-C5 alkyl, none] and R1LN(R2)(CO)_m(CH₂)_nY [R1 = cyclic, bicyclic, tricyclic, benzoheterocyclic, C2-C10 alkyl, tricyclo[3.3.1.03,7]decyl, adamantyl, bicyclo[2.1.2]heptyl, etc.; R2 = H, (aryl)alkyl, mercaptoalkyl, alkenyl, alkynyl, cycloalkyl, aryl, thiazolyl, triazolyl, imidazolyl, benzothiazolyl, benzoimidazolyl, R1R2 = heterocycle; Y = SO₃-X+, OSO₃-X+, SSO₃-X+, X+ = H, cation, ester moiety; m = 0, n = 1-4; L = C1-C3 alkyl, none] that can be used to treat amyloid-related diseases are presented. For example, reacting isopropylamine with 1,3-propanesultone gave 3-isopropylamino-1-propanesulfonic acid in 66% yield. This compound was tested for its ability to bind to β-amyloid and IAPP. The compds. are claimed for their ability to treat or prevent amyloid-related diseases such as Alzheimer's Disease, Down's Syndrome, and macular degeneration.

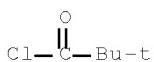
IT 3282-30-2, Pivaloyl chloride

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of compds. to treat amyloid-related diseases)

RN 3282-30-2 HCPLUS

CN Propanoyl chloride, 2,2-dimethyl- (CA INDEX NAME)



IC ICM C07C309-00

CC 21-2 (General Organic Chemistry)

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- Section cross-reference(s): 1, 34, 63
- IT Thyroid gland, neoplasm
(medullary carcinoma; preparation of compds. to treat amyloid-related diseases such as medullary thyroid carcinomas)
- IT Carcinoma
(thyroid medullary; preparation of compds. to treat amyloid-related diseases such as medullary thyroid carcinomas)
- IT 62-57-7, 2-Aminoisobutyric acid 75-31-0, Isopropylamine, reactions 75-64-9, tert-Butylamine, reactions 78-81-9, Isobutylamine 92-54-6, 1-Phenylpiperazine 92-67-1, 4-Aminobiphenyl 96-15-1 103-49-1, Dibenzylamine 103-80-0, Phenylacetyl chloride 107-85-7, Isoamylamine 124-68-5, 2-Amino-2-methyl-1-propanol 585-32-0, Cumylamine 594-39-8, tert-Amylamine 598-74-3, 1,2-Dimethylpropylamine 616-24-0, (1-Ethylpropyl)amine 622-78-6, Benzyl isothiocyanate 665-66-7, 1-Adamantanamine hydrochloride 765-30-0, Cyclopropylamine 822-98-0, 2-Aminonorbornane 1003-03-8, Cyclopentylamine 1011-15-0, 1-(2-Fluorophenyl)piperazine 1120-71-4, 1,3-Propanesultone 1121-03-5, 2,4-Butane sultone 1609-86-5, tert-Butyl isocyanate 1633-82-5, 3-Chloropropane-1-sulfonyl chloride 1633-83-6, 1,4-Butanesultone 1978-61-6, 4-(4-Fluorophenyl)-1,2,3,6-tetrahydropyridine hydrochloride 2026-48-4 2057-49-0, 4-(3-Phenylpropyl)pyridine 2164-19-4, cis-2-Methylcyclohexylamine 2252-63-3, 1-(4-Fluorophenyl)piperazine 2516-34-9, Cyclobutylamine 2577-40-4 2620-50-0, Piperonylamine 2969-81-5, Ethyl 4-bromobutyrate 2975-41-9, 2-Aminoindan 3014-80-0, L-Valinamide hydrochloride 3066-44-2, Diphenylmethyl isocyanate 3081-24-1 3173-56-6, Benzyl isocyanate 3182-95-4, (S)-(-)-2-Amino-3-phenyl-1-propanol 3218-02-8, Cyclohexanemethylamine 3234-64-8, 1,1-Diethylpropargylamine 3282-30-2, Pivaloyl chloride 3395-91-3, Methyl 3-bromopropionate 3674-06-4 3687-18-1, 3-Amino-1-propanesulfonic acid 4202-38-4 4393-09-3, 2,3-Dimethoxybenzylamine 4411-25-0, 1-Adamantyl isocyanate 5267-64-1, (R)-(+)-2-Amino-3-phenyl-1-propanol 5370-01-4, Mexiletine hydrochloride 5452-35-7, Cycloheptylamine 5763-61-1, 3,4-Dimethoxybenzylamine 5813-64-9, Neopentylamine 6269-89-2, 1-(4-Nitrophenyl)piperazine 6321-23-9, 4-Methylcyclohexylamine 7013-33-4 7568-93-6, (±)-2-Amino-1-phenylethanol 10277-74-4, (R)-(-)-1-Aminoindan 10315-03-4, 4-Acetyl-4-phenylpiperidine hydrochloride 10523-68-9, 2-Aminoadamantane hydrochloride 14610-37-8, N-Methyl-tert-butylamine 14650-46-5 15687-27-1, Ibuprofen 15901-42-5, 3,3,5-Trimethylcyclohexylamine 18638-99-8, 3,4,5-Trimethoxybenzylamine 20781-21-9, 2,4-Dimethoxybenzylamine hydrochloride 22038-86-4, (R)-(+)-1-(4-Methoxyphenyl)ethylamine 24250-85-9, 4-Iodo-L-phenylalanine 25611-78-3, 1,2-Diphenylethylamine 30389-18-5, 1-Ethynylcyclohexylamine 34967-24-3, 3,5-Dimethoxybenzylamine 37143-54-7, 2-Amino-1-methoxypropane 38510-87-1 38869-46-4, 1-(4-Chlorophenyl)piperazine dihydrochloride 39512-49-7, 4-(4-Chlorophenyl)-4-piperidinol 41851-59-6 42195-92-6, 2,3-Dimethylcyclohexylamine 43064-12-6, 4-Phenyl-1,2,3,6-tetrahydropyridine hydrochloride 51304-58-6, 4-Cyano-4-phenylpiperidine hydrochloride 51304-61-1 51594-34-4 53329-36-5 57988-58-6, 4-(4-Bromophenyl)-4-piperidinol 61341-86-4, (S)-1-Aminoindan 64715-81-7 69460-11-3 73918-56-6, 4-Bromophenethylamine 75315-63-8 136030-00-7, (1R,2S)-1-Amino-2-indanol 734533-05-2 817163-56-7
- RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of compds. to treat amyloid-related diseases)
- IT 1978-59-2P, 4-(4-Fluorophenyl)-1,2,3,6-tetrahydropyridine 4540-60-7P, L-Valinamide 10338-69-9P,

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4-Phenyl-1,2,3,6-tetrahydropyridine 13074-39-0P, 2-Aminoadamantane
13122-90-2P 20781-20-8P, 2,4-Dimethoxybenzylamine 30005-58-4P,
4-(4-Chlorophenyl)-1,2,3,6-tetrahydropyridine 34715-60-1P 34798-80-6P,
4-Acetyl-4-phenylpiperidine 38212-33-8P, 1-(4-Chlorophenyl)piperazine
40481-13-8P, 4-Cyano-4-phenylpiperidine 97964-72-2P 158686-46-5P
819862-62-9P 819862-63-0P 819862-64-1P 819862-66-3P 819862-67-4P
819862-68-5P 819862-71-0P 819866-00-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of compds. to treat amyloid-related diseases)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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***** SEARCH HISTORY *****

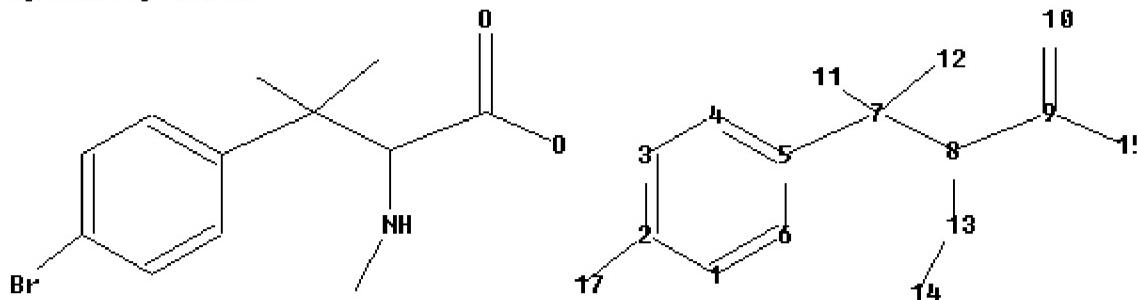
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(FILE 'HOME' ENTERED AT 13:33:41 ON 05 MAR 2009)

FILE 'REGISTRY' ENTERED AT 13:34:00 ON 05 MAR 2009

L1 40598 SEA ABB=ON PLU=ON BROMO? (L) TRIMETHYL?
L2 0 SEA ABB=ON PLU=ON BROMO? (L) TRIMETHYLPHENYLALANIN?
L3 3689 SEA ABB=ON PLU=ON TRIMETHYLPHENYL (L) BROMO?
L4 185 SEA ABB=ON PLU=ON L3 (L) AMINE?
L5 1 SEA ABB=ON PLU=ON "4-BROMO-N" (L) L4
D SCAN
L6 STRUCTURE UPLOADED
D

Uploading L1.str



chain nodes :

7 8 9 10 11 12 13 14 15 17

ring nodes :

1 2 3 4 5 6

chain bonds :

2-17 5-7 7-8 7-11 7-12 8-9 8-13 8-10 9-15 13-14

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :

8-13 9-10 9-15 13-14

exact bonds :

2-17 5-7 7-8 7-11 7-12 8-9

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

isolated ring systems :

containing 1 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 17:CLASS

L7

1 SEA SSS SAM L6

D SCAN

D IDE

FILE 'STNGUIDE' ENTERED AT 13:42:04 ON 05 MAR 2009

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FILE 'REGISTRY' ENTERED AT 13:43:40 ON 05 MAR 2009
L8 88 SEA ABB=ON PLU=ON TETRAMETHYL (L) VALINAMID?
L9 26 SEA ABB=ON PLU=ON L8 (L) TYROSYL
L10 0 SEA ABB=ON PLU=ON L9 (L) ISOPROPYL
L11 21 SEA ABB=ON PLU=ON L9 (L) BUTENYL
L12 16 SEA ABB=ON PLU=ON L11 (L) DIMETHYL?
L13 8 SEA ABB=ON PLU=ON L12 (L) CARBOXY
D SCAN

FILE 'STNGUIDE' ENTERED AT 13:45:29 ON 05 MAR 2009

FILE 'REGISTRY' ENTERED AT 13:51:34 ON 05 MAR 2009
D STAT QUE L6
L14 3 SEA SSS FUL L6
D SCAN
SAVE TEMP L14 JEA722REGL1/A

FILE 'HCAPLUS' ENTERED AT 13:54:11 ON 05 MAR 2009
L15 2 SEA ABB=ON PLU=ON L13
L16 3 SEA ABB=ON PLU=ON L14
L17 3 SEA ABB=ON PLU=ON L15 OR L16
D SCAN TI HIT
E OVARIAN CANCER/CT
E E3+ALL
L18 24595 SEA ABB=ON PLU=ON "OVARY, NEOPLASM"/CT
L19 34474 SEA ABB=ON PLU=ON OVAR? (S) (CANCER# OR NEOPLAS? OR TUMOR#
OR TUMOUR#)
L20 0 SEA ABB=ON PLU=ON L17 AND L19
E NEOPLASM?
E NEOPLASM?/CT
E E5+ALL
L21 167483 SEA ABB=ON PLU=ON NEOPLASM/CT
L22 3 SEA ABB=ON PLU=ON L17 AND L21
L23 1 SEA ABB=ON PLU=ON US20040121965/PN
SEL RN

FILE 'REGISTRY' ENTERED AT 14:00:31 ON 05 MAR 2009
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/BI OR 112898-23-4/BI OR 114-76-1/BI OR 114977-28-5/BI OR
120944-75-4/BI OR 127106-02-9/BI OR 128437-36-5/BI OR 128437-66
-1/BI OR 128437-74-1/BI OR 13139-15-6/BI OR 13734-34-4/BI OR
13781-71-0/BI OR 138802-17-2/BI OR 145432-51-5/BI OR 151-10-0/B
I OR 151-18-8/BI OR 15504-41-3/BI OR 156-06-9/BI OR 160785-01-3
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228266-49-7/BI OR 23082-30-6/BI OR 25080-84-6/BI OR 2605-67-6/B
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OR 66386-16-1/BI OR 676626-71-4/BI OR 676626-79-2/BI OR
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-2/BI OR 676627-

FILE 'HCAPLUS' ENTERED AT 14:02:42 ON 05 MAR 2009

L25 144788 SEA ABB=ON PLU=ON L24
L26 3578 SEA ABB=ON PLU=ON L25 AND (L18 OR L19)
L27 151 SEA ABB=ON PLU=ON "L()VALINAMIDE"
L28 17 SEA ABB=ON PLU=ON L25 AND L27
L29 377 SEA ABB=ON PLU=ON VALINAMIDE
L30 35 SEA ABB=ON PLU=ON L25 AND L29
L31 35 SEA ABB=ON PLU=ON L28 OR L30
L32 0 SEA ABB=ON PLU=ON L31 AND (L18 OR L19)
L33 6 SEA ABB=ON PLU=ON L31 AND (CANCER# OR NEOPLAS? OR TUMOR# OR
TUMOUR# OR CARCIN?)
D SCAN TI HIT

FILE 'STNGUIDE' ENTERED AT 14:07:14 ON 05 MAR 2009

FILE 'REGISTRY' ENTERED AT 14:08:02 ON 05 MAR 2009
L34 1 SEA ABB=ON PLU=ON 676631-40-6/RN
D SCAN

FILE 'HCAPLUS' ENTERED AT 14:09:31 ON 05 MAR 2009
L35 4 SEA ABB=ON PLU=ON L33 NOT L22

FILE 'STNGUIDE' ENTERED AT 14:10:31 ON 05 MAR 2009

FILE 'HCAPLUS' ENTERED AT 14:11:40 ON 05 MAR 2009
L36 84 SEA ABB=ON PLU=ON GREENBERGER L?/AU
L37 34 SEA ABB=ON PLU=ON LOGANZO F?/AU
L38 8 SEA ABB=ON PLU=ON DISCAFANI MARRO C?/AU OR MARRO C?/AU
L39 83 SEA ABB=ON PLU=ON ZASK A?/AU
L40 61 SEA ABB=ON PLU=ON AYRAL KALOUSTIAN S?/AU OR KALOUSTIAN S?/AU

L41 3 SEA ABB=ON PLU=ON (((L36 OR L37 OR L38 OR L39 OR L40)) AND
L16) OR (L16 AND L23)
L42 0 SEA ABB=ON PLU=ON L41 NOT (L17 OR L22)
L43 3 SEA ABB=ON PLU=ON L41 OR L22
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D QUE L43

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FILE 'STNGUIDE' ENTERED AT 14:21:28 ON 05 MAR 2009
D QUE L35

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D L35 1-4 IBIB ABS HITSTR HITIND

FILE 'STNGUIDE' ENTERED AT 14:22:04 ON 05 MAR 2009

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